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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No,	660005.98757
First Inventor or Application Identified	Michael C. Barney et al.
Title	Use of Hop Acids to Inhibit Growth of S. aureus and Prevent Toxic Shock Syndrome
Express Mail Label No.	EK290771473US

jc490 U.S. PTO 09/664679 09/18/00

APPLICATION ELEMENTS
See MPEP Chapter 600 concerning utility patent application contents.

ADDRESS TO: **Assistant Commissioner for Patents**
Box Patent Application
Washington, D.C. 20231

1 [X] Fee transmittal Form
(Submit an original and a duplicate for fee processing)

2 [X] Specification [Total Pages 12]
(preferred arrangement set forth below)
- Descriptive title of the invention
- Cross References to Related Applications
- Statement Regarding Fed Sponsored R&D
- Background of the Invention
- Brief Summary of the Invention
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3 [ ] Drawing(s) (35 USC 113) [Total Sheets]

4. Oath or Declaration [Total Pages]
a. [X] Newly unexecuted (original or copy)
b. [ ] Copy from prior Application (37 CFR 1.63(d)) (for continuation/divisional with Box 17 completed)
[Note Box 5 below]
i. [ ] DELETION OF INVENTOR(S) Signed Statement attached deleting inventor(s) named in prior application,

5 [ ] Incorporation By Reference (useable if Box 4b is checked) The entire disclosure of the prior application from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference herein.

6. [ ] Microfiche Computer Program *(Appendix)*

7. Nucleotide and/or Amino Acid Sequence Submission
(if applicable, all necessary)
a. [ ] Computer readable Copy
b. [ ] Paper Copy
c. [ ] Statement Verifying identity of above

ACCOMPANYING APPLICATION PARTS

8 [ ] Assignment Papers (cover sheet & documents)
9 [ ] 37 CFR 3.73(b) Statement (where there is an assignee) [X] Power of Attorney
10 [ ] English Translation Document *(if applicable)*
11 [X] Information Disclosure Statement (IDS)/PTO-1449 [X] Copies of IDS Citations
12 [ ] Preliminary Amendment
13 [X] Return receipt postcard (MPEP 503) *(Should be specifically itemized)*
14 [ ] *Small Entity Statement(s) [ ] Statement filed in prior application Status still proper and desired
15 [ ] Certified copy of priority Document(s) *(if foreign priority is claimed)*
16 [ ] Other:
* A new statement is required to pay small entity fees, except where one has been filed in a prior application and is being relied upon

17. If a CONTINUING APPLICATION, *check appropriate box and supply the requisite information:*
[ ] Continuation [ ] Divisional [ ] Continuation-in-part (CIP) of prior application no. _____
Prior application information: Examiner: Group/Art Unit:

18. CORRESPONDENCE ADDRESS

[ ] Customer Number or Bar Code Label (Insert Customer No. or Attach bar code label) o [X] Correspondence address below

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Signature		Date	9-18-2000

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FEE TRANSMITTAL

Patent fees are subject to annual revision.
Small Entity payments must be supported by a small entity statement
otherwise large entity fees must be paid, See Forms PTO/SB/09-12
See 37 C.F.R. §§1.27 and 1.28

TOTAL AMOUNT OF	$ 690.00

Complete if Known	
Application Number	
Filing Date	herewith
First Named Inventor	Michael C. Barney
Group Art Unit	
Examiner Name	
Attorney Docket Number	660005.98757

METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge indicated fees and credit any over payments to:

Deposit Account Number: 17-0055

Deposit Account Name: Quarles & Brady LLP

[X] Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17 [ ] Charge the Issue Fee Set in 37 CFR 1.18 at the Mailing of the Notice of Allowance, 37 CFR 1.311(b)

2. [ ] Payment Enclosed: [ ] Check [ ] Money Order [ ] Other

FEE CALCULATION (fees effective 11/10/98)

1. FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	690	201	345	Utility filing fee	690.00
106	310	206	155	Design filing fee	
107	480	207	240	Plant filing fee	
108	690	208	345	Reissue filing fee	
114	150	214	75	Provisional filing fee	

SUBTOTAL (1) ($) 690.00

2. CLAIMS

		Extra		Fee from below		Fee Paid
Total Claims	14	-20**= 0	X		=	
Independent Claims	3	-3**= 0	X		=	
Multiple Dependent Claims					=	

** or number previously paid, if greater, For reissues see below

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	09	Claims in excess of 20
102	78	202	39	Independent claims in excess of 3
104	260	204	130	Multiple dependent claim
109	78	209	39	**Reissue independent claims over original patent
110	18	210	09	**Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)		Fee
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for reexamination	
112	*920	112	*920	Requesting publication of SIR prior to Examiner action	
113	*1,840	113	*1,840	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	380	216	190	Extension for reply within second month	
117	870	217	435	Extension for reply within third month	
118	1,360	218	680	Extension for reply within fourth month	
128	1,850	228	925	Extension for reply within fifth month	
119	300	219	150	Notice of Appeal	
120	300	220	150	Filing a brief in support of an appeal	
121	260	221	130	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive unavoidably abandoned application	
141	1,210	241	605	Petition to revive unintentionally abandoned application	
142	1,210	242	605	Utility issue fee (or reissue)	
143	430	243	215	Design issue fee	
144	580	244	290	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Petitions related to provisional applications	
126	240	126	240	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	690	246	345	Filing a submission after final rejection (37 CFR 1.129(a))	
149	690	249	345	For each additional invention to be examined (37 CFR 1.129(b))	

Other fee (specify) _____

Other fee (specify) _____

SUBTOTAL (3) ($)

* Reduced by Basic Filing Fee Paid

SUBMITTED BY				Complete (if applicable)	
Typed or Printed Name	David M. Kettner	Registration No. (Attorney/Agent)	45,589	Telephone No.	608/251-5000
Signature		Date	September 12, 2000		

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September 18, 2000

Commissioner of Patents
Box Patent Application
Washington DC 20231

Re: Filing New Patent Application

Dear Sir:

Enclosed for filing please find a new patent application entitled: USE OF HOP ACIDS TO INHIBIT THE GROWTH OF STAPHYLOCOCCUS AUREUS AND PREVENT TOXIC SHOCK SYNDROME

by Michael C. Barney
Alfonso L. Navarro
David S. Ryder

The undersigned hereby certifies that this document is being deposited with the United States Postal Service today, June 5, 2000, by the "Express Mail" service, utilizing Express Mail label number EK290771473US addressed to: Commissioner for Patents, Box Patent Application, Washington, DC 20231.

Please indicate receipt of this application by returning the attached postcard with the official Patent and Trademark Office receipt and serial number stamped thereon.

Respectfully submitted,

QBMAD1\225855

USE OF HOP ACIDS TO INHIBIT GROWTH OF STAPHYLOCOCCUS AUREUS AND PREVENT TOXIC SHOCK SYNDROME

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority from provisional patent application Serial No. 60/158,810, filed October 12, 1999.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

Not applicable.

BACKGROUND OF THE INVENTION

The present invention relates to the use of compounds to affect the growth of certain bacterial species. More specifically, the present invention relates to the use of tetrahydroiso alpha acids or hexahydro beta acids at concentrations effective to kill, inhibit, or otherwise control the growth or proliferation of *Staphylococcus aureus* without preventing the growth of *Lactobacillus*. The inhibition of *S. aureus* in accordance with the present invention thus provides useful products, compositions and methods for treating the diseases associated with *S. aureus* infections and infestations, i.e., toxic shock syndrome, without disrupting the normal bacterial flora in the area of its application.

A commonly known disease caused by *S. aureus* is toxic shock syndrome (TSS). TSS is a severe, toxin-induced disease arising from the exposure to the *S. aureus* toxin called toxic shock syndrome toxin-1 (TSST-1) (Iandolo, Ann. Rev. of Micro. 43:275-402, 1989). The disease is characterized by a sudden onset of symptoms, including high fever, chills, rash, vomiting or diarrhea, and a rapid drop in blood pressure leading to shock.

Toxic shock syndrome has been reported to occur in both men and women of all ages, with approximately two cases occurring annually per 10,000 people. TSS, however, is most commonly seen in menstruating women in whom the primary site of infection is the vagina. Epidemiological evidence especially suggests that women who

use highly absorbent tampons incur an increased risk for developing the disease as the highly absorbent tampon serves as an suitable environment for *S. aureus* growth. TSS has also been reported to occur in infants, children, men, and non-menstruating women, but at a lower frequency. These cases are generally not associated with the use of tampons, but result from skin wounds or infections in other parts of the body. The use of barrier contraceptives has also been implicated as another risk factor.

Because of the sudden onset of the disease, persons suffering from TSS may not receive appropriate medical intervention before serious complications result. Such complications may include kidney failure, heart failure, liver failure and profound shock. Accordingly, there is a very strong emphasis on disease prevention. For example, women are cautioned against using high absorbency tampons. However, many women are not willing to sacrifice the comfort and convenience of using high absorbency tampons for what they perceive to be a remote risk of developing TSS. Therefore, considerable effort has been directed toward developing new tampons capable of reducing the risk of contracting TSS as compared to conventional tampons.

Various approaches for preventing toxic shock syndrome from tampon use have been advanced. One such method includes incorporating bactericidal or bacteriostatic agents (i.e., antibiotics or phenol) into the tampon to inhibit *S. aureus* growth. Other methods include the incorporation of agents which prevent the production of TSST-1 or inactivate TSST-1. For example, U.S. Patent 4,405,323 discloses the incorporation of an antibacterial agent, such as povione-iodine, mercury, zinc, penicillin, erythromycin, and nitrofurazone, within a tampon to prevent TSS. U.S. Patent 4,431,427 discloses the incorporation of a water-soluble acid (i.e., citric, glycolic, malic, tartaric, or lactic acid) in a tampon at an amount sufficient to maintain a pH of 4.5 or less in the fluids absorbed by the tampon so as to inhibit the growth of pathogenic bacteria. PCT publication WO 86/05388 discloses that the inclusion of a nontoxic divalent cation, such as magnesium, barium, calcium, strontium, or the like, in an absorptive pad has the effect of inhibiting the production of TSST-1 by *S. aureus*. U.S. Patent 4,585,792 discloses that L-ascorbic acid may be delivered on a tampon to the vaginal area so as to inactivate the toxins associated with TSS. U.S. Patent 5,389,374 discloses that the production of *S. aureus* enterotoxins can be inhibited by exposing the bacterium to an absorbent material treated with either a mono- or diester of apolyhydric aliphatic alcohol.

Although the use of some of these approaches have proven effective in inhibiting the growth of *S. aureus* and TSS, their use may also be problematic. For example, exposing a bacterial population to antibiotics may select for antibiotic resistant mutants, and decrease the efficacy of the antibiotic in treating future infections. In addition, the inclusion of conventional antibiotics will likely result in a considerable increase in cost

to the consumer. Moreover, the use of antibiotics or other bactericidal or bacteriostatic agents may have the undesirable effect of disrupting the normal bacterial flora present in their area of application, ultimately resulting in the onset of other bacterial infections and diseases. For example, *Lactobacillus* is one of the predominant bacteria among normal vaginal flora. The administration of a compound which inhibits *Lactobacillus* may also have the added affect of promoting the establishment of other, less desirable microorganisms which are also present in the vagina. For instance, a low number of *Candida albicans* may be present in the vagina of many healthy asymptomatic women. The administration of a compound which inhibits the growth of *Lactobacillus* may also have the added affect of allowing *C. albicans* to grow and predominate, resulting in a yeast infection.

It would be advantageous, therefore, to have a method for preventing TSS which does not affect normal bacterial flora, and does not allow for the selection of antibiotic resistant bacteria, and does not result in a substantial increase in the overall cost to the consumer. In particular, what is needed is a relatively inexpensive method for inhibiting the growth of *S. aureus* without preventing the growth of *Lactobacillus* or other normal microflora.

BRIEF SUMMARY OF THE INVENTION

The present invention is summarized in that certain compounds are disclosed which are capable of affecting the growth of *Staphylococcus aureus* without preventing the growth of *Lactobacillus* when applied in certain concentrations. These compounds are selected from the group consisting of tetrahydroiso alpha acids, hexahydro beta acids, and salts, mixtures or combinations thereof, and are applied in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*. An effective amount of such compounds, for example, includes a concentration in the range of from about 0.2 ppm to about 25 ppm, or more preferably in the range of from about 0.5 ppm to about 12.5 ppm.

In addition, the present invention includes a product comprising an absorbent material and a compound selected from the group consisting of tetrahydroiso alpha acids, hexahydro beta acids, salts thereof, and mixtures thereof, in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*. The material may include, for example, cellulosic fiber material such as those typically used in feminine hygiene products (i.e., feminine napkins, tampons, etc.), or used to absorb bodily fluids or apply compounds employed in preventing or treating bacterial infections.

The present invention also includes a composition comprising a pharmaceutically acceptable carrier, and a compound selected from the group consisting of tetrahydroiso alpha acids, hexahydro beta acids, salts thereof, and mixtures thereof, in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*. The carrier may include, for example, topical ointments or washes formulated to facilitate effective administration of the compound.

It is an object of the present invention to provide a compound having inhibitory activity against *S. aureus* and minimal to no inhibitory activity against *Lactobacillus* when applied at certain concentrations.

It is also an object of the present invention to provide products and compositions for contacting *S. aureus* with such a compound.

It is yet another object of the invention to provide a method for preventing or treating *S. aureus* infection or infestation.

Other objects, advantages and features of the present invention will become apparent from the following detailed description and examples.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

Not applicable.

DETAILED DESCRIPTION OF THE INVENTION

The present invention discloses compounds which, when applied at certain concentrations, affect the growth of *Staphylococcus aureus* without preventing the growth of *Lactobacillus*. The compounds are selected from the group consisting of tetrahydroiso alpha acids, hexahydro beta acids, salts thereof, and mixtures thereof, and may be combined with various materials or carriers to form products and compositions suitable for facilitating effective administration. The present invention also discloses methods for using the compounds to prevent or treat *S. aureus* infection or infestation without disrupting the normal flora of *Lactobacillus* in its area of application.

We have discovered that the hop acids tetrahydroiso alpha and hexahydro beta have unexpectedly different bacteriocidal or bacteriostatic effects against *Lactobacillus* as compared to *S. aureus*. Specifically, *Lactobacillus* and *S. aureus* exhibit a differing level of sensitivity to tetrahydroiso alpha and hexahydro beta acids, with *S. aureus* being more sensitive than *Lactobacillus*. As a result, it is now possible to selectively inhibit *S. aureus* without preventing the growth of *Lactobacillus* by contacting the *S. aureus* with an amount of tetrahydroiso alpha acid or hexahydro beta acid which effectively inhibits *S. aureus* while allowing *Lactobacillus* to continue to grow.

The primary embodiment of the present invention is to provide a method for inhibiting *S. aureus* infection or infestation by contacting the *S. aureus* environment with an effective concentration of a compound which kills, inhibits, or otherwise controls the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*. In the preferred embodiment, the *S. aureus* environment is exposed to an effective concentration of the compound in a range of from about 0.2 ppm to about 25 ppm, and more preferably, in a range of from about 0.5 ppm to about 12.5 ppm.

As used herein, the term "compound" is intended to include hexahydro beta acids, hexahydro beta salts, tetrahydroiso alpha acids, tetrahydroiso alpha salts, and mixtures or combinations thereof.

To affect the growth of *S. aureus*, the compound may be placed in contact with a *S. aureus* environment either independently or as part of a composition or product wherein the composition or product contains an effective amount of the compound in accordance with the present invention. In another embodiment, the compound may be layered or coated onto a barrier type contraceptive such as a diaphragm or contraceptive sponge that is placed in the *S. aureus* environment. The *S. aureus* environment may include, for example, any environment having a population of the *S. aureus* bacterium or an environment capable of allowing *S. aureus* to grow and proliferate. For instance, the environment may include, without limitation, wounds, lesions, tampons, the vagina, sanitary napkins, gauze, diapers, suppositories, or any other possible areas susceptible to *S. aureus* infection or infestation.

As used herein, the term "product" includes those products capable of, either inherently or by virtue of the manner in which they are assembled, absorbing liquids such as water, urine, menstrual fluids, blood, wound exudates and the like. Such products include, for example, catemenial products (e.g. tampons), wound dressings, suppositories, disposable diapers, and sanitary napkins, in addition to other kinds of tampons intended for medical, surgical, dental and/or nasal use. Products according to the present invention may be prepared according to known methods for manufacturing such products. In general, the products should be prepared to allow an effective amount of the compound utilized to be placed in contact with the *S. aureus* environment.

In one embodiment, the product comprises of an absorbent material and an amount of compound which effectively kills, inhibits, or otherwise controls the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus* when said product is exposed to the *S. aureus* environment. A used herein, the term "absorbent material" includes, without limitation, natural fibers or synthetic fibers, films, foams, wood, pulp, peat moss, superabsorbent polymers and the like which are capable of, either inherently or by virtue of the manner in which they are assembled, absorbing

liquids such as water, urine, menstrual fluids, blood, wound exudates and the like.

The term "composition" includes those compositions capable of, either inherently or by virtue of their formulation, use as a topical ointment or wash applied to a wound, infection, or the like. Compositions may be formulated according to known methods for preparing pharmaceutically useful compositions. Formulations are described in detail in a number of sources which are well known and readily available to those skilled in the art. For example, *Remington's Pharmaceutical Science*, by E.W. Martin describes formulations which can be used in connection with the subject invention. In general, the compositions should be formulated such that an effective amount of the compound utilized is combined with the suitable carrier in order to facilitate effective administration.

In one embodiment, the composition consists of a douche for killing, inhibiting, or otherwise controlling the growth or proliferation of *S. aureus* in the vagina. This is particularly useful for providing a treatment to a woman to help fight against *S. aureus* infection or infestation that can cause toxic shock syndrome. Alternatively, the composition may be formulated as a topical ointment or wash for application to wounds or infections in other parts of the body.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof are to be included within the spirit and purview of this application and the scope of the appended claims. Following are examples which are intended to be purely illustrative, and should not be construed as limiting but merely exemplary.

EXAMPLES

Minimal inhibitory concentration (MIC) assays of several hop compounds were conducted using a *Staphylococcus aureus* species and vaginal isolates *Lactobacillus vaginalias*, *Lactobacillus crispatus*, *Lactobacillus gasseri*, and *Lactobacillus jensenii* as test microorganisms. *Lactobacillus* assays were conducted in Lactobacillus MRS broth (Difco) tubes. A 0.1 ml aliquot of a 1% (w/w) solution of each hop acid in alcohol was added to a tube of sterile MRS broth to give a final concentration of 100 ppm of the hop. This solution was serially diluted in tubes with sterile MRS broth using a two-fold dilution series. A second dilution series prepared as above, but using 0.1 ml alcohol without hop acid, was used as a positive control of bacterial growth. Each tube was inoculated with a fresh culture (10^4 cells) of a *Lactobacillus* species in MRS broth. The cultures were incubated anaerobically in a CO_2 incubator at 28°C for five days. Growth was evaluated by visually assessing and scoring development of turbidity in the tube of

broth.

The MIC assays for *Staphylococcus aureus* were conducted in Difco trypticase soy broth (TSB) using the same serial dilution technique and the inoculum level as described above. The pH of the TSB was adjusted to pH 7.0, pH 6.0, or pH 5.0 using hydrochloric acid. The tubes were incubated aerobically at 37°C for three days and growth was evaluated by visually assessing and scored the development of turbidity in the broth.

The results of MIC assay of tetrahydroiso alpha acids and hexahydro beta acids on *S. aureus* and *Lactobacillus* are shown in Tables 1 and 2, respectively. As illustrated by a comparison of Tables 1 and 2, it is evident that *S. aureus* is much more sensitive to tetrahydroiso alpha acids and hexahydro beta acids than the *Lactobacillus* species tested. In particular, *Lactobacillus* exhibited strong growth in concentrations of hexahydro beta acid and tetrahydroiso alpha acid as high as 12.5 ppm. In contrast, *S. aureus* showed no to very weak growth in tetrahydroiso alpha acid or hexahydro beta acid concentrations as low as 1.56 ppm. The sensitivity of *S. aureus* also appeared to increase under acidic conditions, with the minimum inhibitory concentration decreasing to 0.78 ppm at pH 6.0 and to less than 0.2 ppm at pH 5.0. Normally, the pH of the vagina is in the range of about 4.5 to 5.0.

Table 1

MIC Assays of Tetrahydroiso Alpha Acids and Hexahydro Beta Acids using *Staphylococcus aureus*						
	TSB at pH 7.0		**TSB at pH 6.0**		**TSB at pH 5.0**	
Concentration (ppm)	**Tetra**	**Hexa**	**Tetra**	**Hexa**	**Tetra**	**Hexa**
100	No growth	No growth	No growth	No growth	No growth	No growth
50	No growth	No growth	No growth	No growth	No growth	No growth
25	No growth	No growth	No growth	No growth	No growth	No growth
12.5	No growth	No growth	No growth	No growth	No growth	No growth
6.25	No growth	No growth	No growth	No growth	No growth	No growth
3.125	No growth	No growth	No growth	No growth	No growth	No growth
1.56	+/- Growth	+/- Growth	No growth	No growth	No growth	No growth
0.78	+ Growth	+ Growth	No growth	No growth	No growth	No growth
0.39	++ Growth	++ Growth	+/- Growth	No growth	No growth	No growth
0.2	+++ Growth	+++ Growth	++ Growth	+ Growth	No growth	No growth
0	+++ Growth	+++ Growth	+++ Growth	+++ Growth	+++ Growth	+++ Growth

Table 2.

MIC Assays of Tetrahydroiso Alpha Acids and Hexahydro Beta Acids using *Lactobacillus* species		
	MRS at pH 6.3	
Concentration (ppm)	Tetra	Hexa
100	No growth	No growth
50	No growth	No growth
25	+/- Growth	+/- Growth
12.5	++ Growth	+++ Growth
6.25	+++ Growth	+++ Growth
3.125	+++ Growth	+++ Growth
1.56	+++ Growth	+++ Growth
0.78	+++ Growth	+++ Growth
0.39	+++ Growth	+++ Growth
0.2	+++ Growth	+++ Growth
0	+++ Growth	+++ Growth

CLAIMS

WE CLAIM:

1. A method for affecting the growth of *Staphylococcus aureus*, said method comprising the step of:

contacting an environment containing *S. aureus* with a compound selected from the group consisting of hexahydro beta acids, hexahydro beta salts, tetrahydroiso alpha acids, tetrahydroiso alpha salts, mixtures thereof, and combinations thereof, in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*.

2. The method of claim 1, wherein the concentration of the compound is in the range of from about 0.2 ppm to about 25 ppm.

3. The method of claim 1, wherein the compound is placed in contact with the *S. aureus* environment using a product comprising of an absorbent material and the compound.

4. The method of claim 3, wherein the absorbent material is selected from the group consisting of a natural fiber, a synthetic fiber, a film, a foam, a wood, a pulp, a peat moss, and a superabsorbent polymer.

5. The method of claim 3, wherein the product is selected from the group consisting of a tampon, wound dressing, suppository, disposable diaper, and sanitary napkin.

6. The method of claim 1, wherein the compound is placed in contact with the *S. aureus* environment using a composition comprising of a pharmaceutically acceptable carrier and the compound.

7. The method of claim 6, wherein the compound is either a douche or a topical ointment.

8. The method of claim 1, wherein the compound is placed in contact with the *S. aureus* environment using a barrier contraceptive.

9. A composition comprising a pharmaceutically acceptable carrier, and a compound selected from the group consisting of hexahydro beta acids, hexahydro beta salts, tetrahydroiso alpha acids, tetrahydroiso alpha salts, mixtures thereof, and combinations thereof, in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*.

10. The composition of claim 9, wherein the concentration of the compound is in the range of from about 0.2 ppm to about 25 ppm.

11. The composition of claim 9, wherein the pharmaceutically acceptable carrier is either a douche or a topical ointment.

12. A product comprising an absorbent material, and a compound selected from the group consisting of hexahydro beta acids, hexahydro beta salts, tetrahydroiso alpha acids, tetrahydroiso alpha salts, mixtures thereof, and combinations thereof, in an amount effective to kill, inhibit, or otherwise control the growth or proliferation of *S. aureus* without preventing the growth of *Lactobacillus*.

13. The product of claim 12, wherein the concentration of the compound is in the range of from about 0.2 ppm to about 25 ppm.

14. The product of claim 12, wherein the absorbent material is selected from the group consisting of a natural fiber, a synthetic fiber, a film, a foam, a wood, a pulp, a peat moss, and a superabsorbent polymer.

ABSTRACT OF THE DISCLOSURE

The present invention provides methods, products, and compositions for selectively inhibiting the growth of *Staphylococcus aureus* without preventing the growth of *Lactobacillus* species. Specifically, the present invention discloses the use of tetrahydroiso alpha acid or hexahydro beta acid at a concentration effective to inhibit the growth of *S. aureus* without preventing the growth of *Lactobacillus*. The inhibition of *S. aureus* in accordance with the present invention thus provides useful methods, compositions and products such as feminine hygiene products for treating the diseases associated with *S. aureus* infections and infestations, i.e., toxic shock syndrome, without disrupting the normal bacterial flora in the area of its application.

SEQUENCE LISTING

Not applicable.

PTO/SB/01 (6-95)
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Please type a plus sign (+) inside this box [+]

0010/PTO
Rev. 6/95

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Patent and Trademark Office

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

[X] Declaration Submitted with Initial Filing OR [ ] Declaration Submitted after Initial Filing

Attorney Docket Number	660005.98757
First Named Inventor	Michael C. Barney
COMPLETE IF KNOWN	
Application Number	
Filing Date	Herewith
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I *believe* that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

USE OF HOP ACIDS TO INHIBIT GROWTH OF STAPHYLOCOCCUS AUREUS AND PREVENT TOXIC SHOCK SYNDROME

(Title of the Invention)

the specification of which

[x] is attached hereto

OR

[ ] was filed on (MM/DD/YY) [ ] as United States Application Number or PCT International

Application Number [ ] and was amended on (MM/DD/YY) [ ] (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YY)	Priority Not Claimed	Certified Copy Attached? YES	NO
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]

[ ] Additional foreign applications numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YY)	
60/158,810	10/12/99	[ ] Additional provisional

Burden Hour Statement: This form is estimated to take .4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.
QBMAD1\225850

Please type a plus sign (+) inside this box [+]

DECLARATION

I hereby claim benefit under Title 35, United States Code §120 of any United States application(s), or §365(C) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application or PCT international application in the manner provided in the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YY)	Parent Patent Number *(if applicable)*

[ ] Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and all continuation and divisional applications based thereon, and to transact all business in the Patent and Trademark Office connected therewith:

[ ] Firm Name _____ Customer Number or label _____
OR
[X] List attorney(s) and/or agent(s) name and registration number below

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[ ] Additional attorney(s) and/or agents named on a supplemental priority sheet attached hereto

Please direct all correspondence to [ ] Customer Number or label _____ OR [X] Fill in correspondence address below

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Name of Sole or First Inventor: [ ] A petition has been filed for this unsigned inventor

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[ ] Additional inventors are being named on supplemental sheet(s) attached hereto

Please type a plus sign (+) inside this box [+]

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet

Name of Additional Joint Inventor, if any: | A petition has been filed for this unsigned inventor

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Inventor's Signature | Date

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City	State	Zip	Country	Applicant Authority

[ ] [ ] Additional inventors are being named on supplemental sheet(s) attached hereto